

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Office Action states:

The originally filed specification and claims provide insufficient written description support for the new claimed recitation drawn to isolated polypeptides having aminopeptidase activity further having physicochemical properties of "an ability to hydrolyze a substrate containing Ala, Arg, Asn, ... Val at its N-terminus" as recited in said new claims 46-89.

This rejection is respectfully traversed.

The specification on page 4, lines 2-8, provides support for the recitation "an ability to hydrolyze a substrate containing Ala, Arg, Asn, ... Val at its N-terminus" in claims 46-89. These claims have been cancelled and rewritten as claim 90-129.

For the foregoing reason, Applicants submit that the rejections under 35 U.S.C. § 112, first paragraph, have been overcome and respectfully request reconsideration and withdrawal of the rejections.

II. The Rejection of Claims 46-89 under 35 U.S.C. § 112, First Paragraph

Claims 46-89 stand rejected under 35 U.S.C. § 112, first paragraph, "as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention." Specifically, the Office Action states:

The claimed invention is drawn to isolated polypeptides having aminopeptidase activity and having "amino acid sequence which has at least 70%/80%/90%/95%/97% identity" with claimed SEQ ID NOs.

The specification does not support the broad scope of the claims which encompass a multitude of analogs because the specification does not disclose the following: the general tolerance to modification and extent of such tolerance with regard to effects of amino acid substitutions, deletions and/or insertions on claimed aminopeptidase activity; specific positions which can be predictably modified; and the specification provides essentially no guidance as to which of the essentially infinite possible choices is likely to be successful.

This rejection is respectfully traversed.

Applicants' contribution to the art is the discovery of a polypeptide having aminopeptidase activity, wherein the polypeptide has the ability to hydrolyze a proteinaceous substrate containing Ala, Arg, Asn, Asp, Cys, Gln, Glu, Gly, His, Ile, Leu, Lys, Phe, Pro, Ser, Thr, Trp, Tyr, or Val at its N-terminus. Moreover, Applicants have provided detailed

instructions on how to obtain such polypeptides and nucleic acid sequences encoding such polypeptides. Applicants' specification provides adequate guidance for finding such analogs encoded by a nucleic acid as detailed on page 4, line 9, to page 6, line 17, of the specification. Furthermore, hybridization conditions and protocols are defined on page 5, line 18, to page 6, line 18, of the specification. On the basis of Applicants' disclosure, one skilled in the art would know how to identify and isolate such analogs. Applicants, therefore, submit that the information disclosed in the specification provides sufficient guidance to one skilled in the art to isolate an analog of the claimed polypeptides where one or more amino acids are changed. Moreover, a polypeptide having an amino acid sequence which has at least 70%, 80%, 90%, 95%, or 97% identity with and retains the properties of the claimed polypeptides could be identified using Applicants' disclosure. However, to further prosecution, new claim 90, which corresponds to cancelled claim 46, recites "90% identity".

For the foregoing reason, Applicants submit that the rejections under 35 U.S.C. § 112, first paragraph, have been overcome and respectfully request reconsideration and withdrawal of the rejections.

III. The Rejection of Claims 46-90 under 35 U.S.C. § 112, Second Paragraph

Claims 46-90 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The office actions states:

The specification (page 4) refers to the use of "the Clustal method" with an "identity table" to measure sequence identity. However the specification fails to clearly point out the parameters or properties of said "identity table". Absent definite and clear parameters or description of said Clustal method identity table to determine percent identity of two sequences, use of said identity table could result in inconsistent assessment of sequence identity absent clear recitation of the parameters, and the metes and bounds of the sequences as instantly claimed can not be ascertained.

This rejection is respectfully traversed.

Applicants pointed out in the amendment of June 3, 1999, that percent identity is measured by the Clustal method using the parameters described on page 4, lines 18-20, of the specification. The Clustal method is well known in the art for determining sequence alignments as described by Higgins *et al.* in *CABIOS* 5: 151-153 (1989). However, there appears to be a misunderstanding regarding the identity table. The identity table is simply the

result of the determination of the percent identity of two more sequences by the Clustal method using the parameters described on page 4, lines 18-20, of the specification.

For the foregoing reason, Applicants submit that the new claims overcome the rejections under 35 U.S.C. § 112, second paragraph. Applicants respectfully request reconsideration and withdrawal of the rejection.

IV. The Rejection of Claims 64-67 under 35 U.S.C. § 112, Second Paragraph

Claims 64-67 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for reciting the limitation "the polypeptide of claim 1" because there is insufficient antecedent basis for this limitation in the claims since claim 1 has been cancelled by applicants.

Applicants have canceled claim 64-67 rendering the rejection moot, but have taken this rejection into consideration in new claims 90-129.

For the foregoing reason, Applicants submit that the new claims overcome the rejections under 35 U.S.C. § 112 and respectfully request reconsideration and withdrawal of the rejection.

V. The Rejection of Claims 17-20 and 22-24 under 35 U.S.C. § 102

Claims 46, 52, 56-63, and 69 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Holm *et al.* (U.S. Patent No. 5,821,104). The Office Action states:

[A]pplicants arguments are not persuasive since applicants arguments are not commensurate in scope with the claimed invention, i.e., said claims do not claim aminopeptidase "which sequentially removes one amino acid residue at a time from the N-terminus". Further, applicants arguments that aminopeptidase is not tripeptidyl aminopeptidase are not commensurate in scope with the claimed invention, since claimed invention is drawn to any isolated polypeptides as claimed "having aminopeptidase activity."

This rejection is respectfully traversed.

Applicants pointed out in the amendment of June 3, 1999, that Holm *et al.* disclose a tripeptidyl aminopeptidase, which sequentially removes intact tripeptides from the N-terminus of a peptide, polypeptide, or protein. (See page 1, lines 20-22 of the Holm *et al.* reference), but Holm *et al.* do not disclose an aminopeptidase which sequentially removes one amino acid residue at a time from the N-terminus of a peptide, polypeptide, or protein, as claimed herein. Applicants also provided a copy of an article by Taylor, 1993, *The FASEB*

Journal 7: 290-298, which defines an aminopeptidase (see page 290, column 2, first complete paragraph), which showed that the term "aminopeptidase" to one skilled in the art is not a tripeptidyl aminopeptidase. However, to further prosecution Applicants have amended the new claims to recite "wherein the polypeptide having aminopeptidase activity sequentially removes one amino acid residue at a time from the N-terminus of a peptide, polypeptide, or protein."

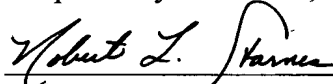
For the foregoing reasons, Applicants submit that this rejection under 35 U.S.C. § 102 has been overcome. Applicants respectfully request reconsideration and withdrawal of the rejection.

VI. Conclusion

In view of the above, it is respectfully submitted that all claims are in condition for allowance. Early action to that end is respectfully requested. The Examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this amendment or application.

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Respectfully submitted,



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